Original Article

Timing of silicone stent removal in patients with post-tuberculosis bronchial stenosis

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Abstract:

CONTEXT: In patients with post-tuberculosis bronchial stenosis (PTBS), the severity of bronchial stenosis affects the restenosis rate after the silicone stent is removed. In PTBS patients with incomplete bronchial obstruction, who had a favorable prognosis, the timing of stent removal to ensure airway patency is not clear.

AIMS: We evaluated the time for silicone stent removal in patients with incomplete PTBS.

SETTINGS AND DESIGN: A retrospective study examined PTBS patients who underwent stenting and removal of a silicone stent.

METHODS: Incomplete bronchial stenosis was defined as PTBS other than total bronchial obstruction, which had a luminal opening at the stenotic segment on bronchoscopic intervention. The duration of stenting was defined as the interval from stent insertion to removal. The study included 44 PTBS patients and the patients were grouped at intervals of 6 months according to the duration of stenting.

RESULTS: Patients stented for more than 12 months had a significantly lower restenosis rate than those stented for less than 12 months (4% vs. 35%, $P = 0.009$). Multiple logistic regression revealed an association between stenting for more than 12 months and a low restenosis rate (odds ratio 12.095; 95% confidence interval 1.097-133.377). Moreover, no restenosis was observed in PTBS patients when the stent was placed more than 14 months previously.

CONCLUSIONS: In patients with incomplete PTBS, stent placement for longer than 12 months reduced restenosis after stent removal.

Key words:

Airway obstruction, bronchoscopy, device removal, stents, tuberculosis

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Silicone airway stents are an effective treatment option for benign airway stenosis;[1-4] however, long-term stent placement has various complications, such as sputum retention, stent migration and granulation tissue formation.[5] Therefore, after the bronchial strictures have healed, it is important to remove silicone airway stents.

Traditionally, elective stent removal is performed 6-18 months after stent insertion in patients with benign airway stenosis, regardless of etiology, based on expert opinion.[3,6,7] Research on the timing of stent removal in each etiology is needed and some studies using distinct protocols for the timing of stent removal have reported varying outcomes in patients with benign airway stenosis.[6,8] Brichet *et al.* removed silicone airway stents 6 months after stenting in patients with post-intubation tracheal stenosis and reported 70% restenosis after stent removal.[8] Martinez-Ballarin *et al.* performed stent removal after 18 months and restenosis occurred in 19% of patients with benign airway stenosis other than post-tuberculosis strictures.[6] These results suggest that the long-term placement of silicone stents in patients with benign airway stenosis other than post-tuberculosis stenosis reduces the restenosis rate after stent removal. However, no report has examined the timing of silicone airway stent removal in patients with post-tuberculosis bronchial stenosis (PTBS).

Recently, data on the factors allowing successful stent removal in PTBS patients were published.[9] Patients without complete lobar atelectasis on computed tomography (CT) scan at initial presentation had a better prognosis than those with complete atelectasis. Therefore, the completeness of stenosis affects the outcome of bronchoscopic intervention; patients with stenosis severe enough to cause complete atelectasis had a higher restenosis rate (72%) than patients with incomplete stenosis who had no atelectasis (restenosis rate 31%). Although patients with incomplete PTBS had a favorable clinical outcome, the optimal timing of elective stent removal is still unclear. Therefore, this study evaluated the optimal timing of bronchial stent removal in patients with incomplete PTBS.

Methods

Study subjects

This retrospective study enrolled 76 consecutive PTBS patients who underwent bronchoscopic interventions between January 2004 and December 2009 at Samsung Medical Center, the Teaching Hospital of Sungkyunkwan University, Seoul, Korea. The completeness of bronchial stenosis was assessed using bronchoscopy; complete bronchial stenosis was defined as total obstruction of the bronchial lumen due to fibrotic stenosis at bronchoscopy and incomplete bronchial stenosis was defined as PTBS other than complete bronchial stenosis, with a luminal opening at the stenotic segment. Of the 76 PTBS subjects, 57 patients underwent silicone stenting in the main bronchi or bronchus intermedius and the stents were removed in 54 patients [Figure 1]. In the 54 patients who underwent elective stent removal, incomplete and complete bronchial stenosis was found in 44 and 10 patients, respectively. This study considered the 44 patients with incomplete bronchial stenosis. Some of the clinical data on the patients enrolled between 2004 and 2008 were included in articles published in 2011 and 2012.[9,10]

The institutional review board of Samsung Medical Center approved the analyses of the clinical and radiological data. Informed consent was waived because of the retrospective nature of the study.

Therapeutic bronchoscopy

Rigid bronchoscopy was performed using standard techniques as described previously.[7,11,12] A representative case of PTBS is shown in Figure 2. Briefly, the patients were intubated with a rigid Hopkins bronchoscope (Karl-Storz, Tuttlingen, Germany) under general anesthesia. Then airway stenosis was identified based on a detailed examination of the bronchial tree using a flexible bronchoscope (EVIS BF 1T240, Olympus, Tokyo, Japan) introduced through the rigid bronchoscope. After identifying bronchial stenosis, all patients underwent mechanical dilatation using a rigid tube, ballooning (Boston Scientific, Natick, MA) or neodymium: Yttrium-aluminium-garnet laser cauterization (Lasersonics, Milpitas, CA).

After mechanical dilation, a silicone bronchial stent (N-stent; TNO, Seoul, South Korea) was inserted for the following indications: (1) Symptomatic restenosis, including dyspnea, occurred after the first intervention without stenting; (2) bronchomalacia was observed over more than 180° of the dilated lumen, which led to severe dyspnea without stenting (bronchomalcia was assessed visually during rigid bronchoscopy by an interventional pulmonologist) or (3) the longitudinal stenotic segment was longer than 2 cm. The diameters of all implanted stents were 9 mm (inner) and 10 mm (outer). The length of the stent was selected by the interventional pulmonologist.

Elective removal of a bronchial silicone stent

Silicone stent removal was considered once the patients had been stable for more than 6 months and was typically 6-12 months from the initial stenting. The patients were usually discharged from the hospital the day following stent removal.

Definitions and patients grouping

Restenosis after stent removal, i.e., stent removal "failure," was defined as the occurrence of bronchial obstruction after stent removal that needed bronchoscopic intervention. The duration of stenting was defined as the interval from stent insertion to removal. Using the duration of stenting, the study population was grouped at 6-month intervals.

Statistical analysis

All results are presented as numbers (percentage) for categorical variables and medians (interquartile range [IQR]) for continuous variables. Because the data were not distributed normally, non-parametric analyses, such as the Mann-Whitney U-test, were used for continuous variables. Proportions were compared using the Pearson Chi-square test or Fisher's exact test. Following univariate analyses, a logistic regression model was constructed using the variables with $P < 0.1$ in

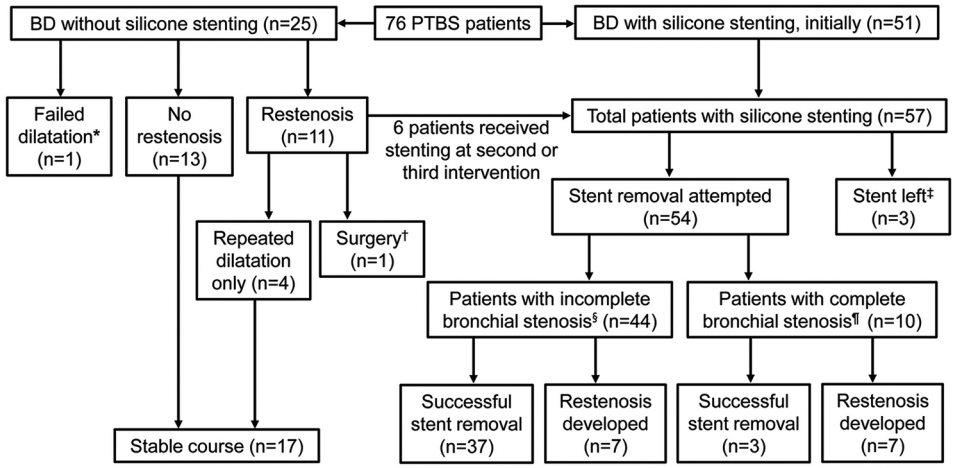

Figure 1: Selection of the study subjects from 76 post-tuberculosis bronchial stenosis patients. *Due to dense fibrosis, mechanical dilatation failed in one patient. †One patient underwent a right upper lobectomy and resection of the right main bronchus with distal carina-bronchus intermedius anastomosis when restenosis developed. ‡Three patients refused stent removal due to concerns regarding restenosis. §Forty-four patients with incomplete bronchial stenosis who underwent elective stent removal were selected for this study and the restenosis rate after stent removal was 16%. ¶Patients with complete bronchial stenosis suffered 70% restenosis after stent removal, which was significantly higher than those with incomplete stenosis ($P = 0.002$). PTBS = Post-tuberculosis bronchial stenosis, BD = Bronchial dilatation

the univariate analyses. Values of $P < 0.05$ were considered to indicate statistical significance. All statistical analyses were performed using the statistical package for the social sciences (SPSS) version 20.0 for Windows (SPSS, Chicago, IL).

Results

The baseline characteristics of the 44 study subjects with incomplete bronchial stenosis are presented in Table 1. A total of 35 patients (80%) presented with dyspnea and all achieved symptomatic improvement immediately following the procedure: Dyspnea disappeared in 27 patients (77%) and improved in 8 (23%). The most common abnormal finding on chest CT was atelectasis: 1 patient (4%) had two-lobe atelectasis and 15 (31%) had one-lobe atelectasis. The median follow-up period after stent removal was 9 (IQR 5-27) months. After the first rigid bronchoscopy, there were 45 additional interventions in 27 patients (61%) and the median intervention interval was 2 (IQR 1-4) months. Of the 44 patients, the duration of stenting was <12, 12-18, and >18 months in 17, 12 and 15 patients, respectively. The overall changes in the pulmonary function tests are presented in Table 2.

Restenosis after stent removal

Of the 44 subjects, 7 (16%) had restenosis after stent removal and the median duration of stenting of all patients was 14 (IQR 10-22) months. The median interval from stent removal to restenosis was 1 (IQR 0-2) month and all restenosis developed within 3 months of stent removal. The restenosis rate after stent removal was 35%, 8% and 0% in patients with duration of stenting <12, 12-18, and >18 months, respectively [Figure 3]. There was a significant difference in the restenosis rate between patients with durations of stenting <12 and >18 months ($P = 0.019$), but no significant difference between patients with duration of stenting <12 and 12-18 months ($P = 0.187$) or 12-18 and >18 months ($P = 0.444$).

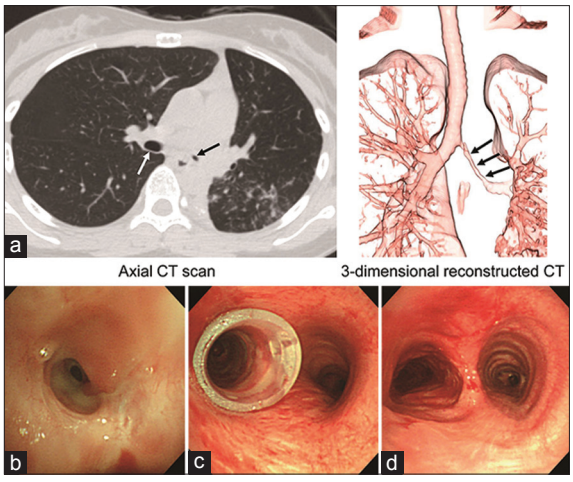

Figure 2: Representative case of post-tuberculosis bronchial stenosis. (a) On chest computed tomography scan, the left main bronchus was narrowed to approximately 2 mm in diameter (black arrow), whereas the right main bronchus showed normal airway patency (white arrow). (b) On bronchoscopy, the left main bronchus was partially obstructed by fibrotic stenosis. (c) After mechanical dilatation, a silicone bronchial stent was inserted into the left main bronchus (inner diameter 9 mm, outer diameter 10 mm, stent length 40 mm). (d) Twenty months after silicone stenting, elective stent removal was performed

Table 1: Baseline characteristics of the 44 study subjects

Characteristics	No. (%) or median (IQR)
Age, years	35 (31-45)
Female gender	36 (82)
Active TB	1 (2)
TB medication at first intervention	9 (21)
Duration of TB treatment, months	6 (6-12)
Initial CT findings, overlapped	
No parenchymal lesion	7 (16)
Atelectasis involving more than one lobe	16 (36)
Consolidation	7 (16)
Nodular lesion	14 (32)
Fibrocalcific lesion	10 (23)
Stenting site	
Left main bronchus	36 (82)
Right main bronchus	3 (7)
Right bronchus intermedius	5 (11)
Modalities for airway dilatation, overlapped	
Ballooning	44 (100)
Laser therapy	3 (7)
Bougienation	1 (2)
Stent length, mm	43 (40-50)
Duration of stenting, months	14 (10-22)
Restenosis after elective stent removal	7 (16)

TB = Tuberculosis, IQR = Interquartile range, CT = Computed tomography

Table 2: Pulmonary function tests of the 44 study subjects

Timing of pulmonary function tests	FEV_1	FVC	FEV_1/FVC
Before stenting*	67 (62-71)	81 (70-92)	65 (54-76)
After stenting	77 (70-90)	92 (79-102)	70 (62-79)
After stent removal†	86 (76-94)	100 (86-108)	67 (59-78)

FEV1 = Forced expiratory volume in 1 s, FVC = Forced vital capacity
*Pulmonary function tests before stent insertion was available in 39 patients, †Pulmonary function tests after stent removal was available in 36 patients

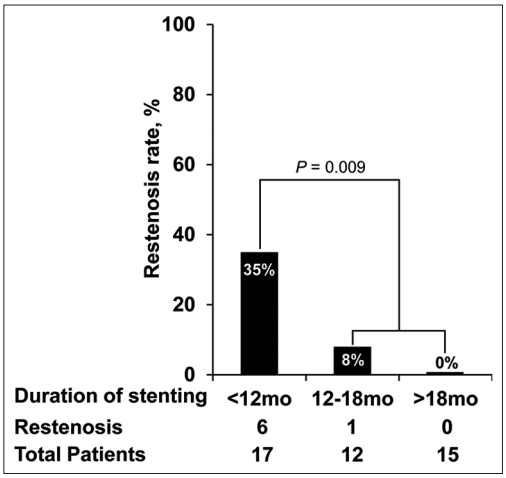

Figure 3: Restenosis rate according to the duration of stenting in post-tuberculosis bronchial stenosis patients with incomplete stenosis. There was an apparent difference in restenosis rate between patients with duration of stenting <12 months and ≥12 months ($P = 0.009$)

Of patients with duration of stenting ≥12 months, only one developed restenosis after stent removal and there was a significant difference in the restenosis rate between patients with durations of stenting <12 and ≥12 months (35% vs. 4%, $P = 0.009$). Moreover, after 14 months from stenting, there was no restenosis after stent removal [Figure 4].

Factors associated with restenosis after stent removal other than stenting duration

To identify the factors contributing to restenosis other than stenting duration, univariate analysis was conducted [Table 3].

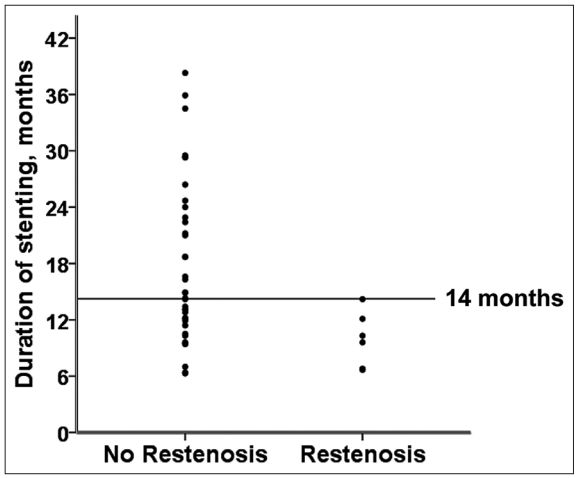

Figure 4: Scatter diagram of restenosis after stent removal and duration of stenting. Patients without restenosis had a median duration of stenting of 15 (interquartile range 12-23) months and all patients who developed restenosis had the stent removed within 14 months of insertion

Patients with restenosis after stent removal were much younger than those without restenosis ($P = 0.027$) and the interval from tuberculosis medication to first intervention was much shorter in patients with restenosis than in those without restenosis, with borderline statistical significance ($P = 0.057$).

Multiple logistic regression analysis of restenosis after stent removal

Multiple logistic regression analysis was performed to determine whether stenting duration >12 months was independently associated with the outcome after stent removal. This revealed an association between the stent placement >12 months and a lower restenosis rate after stent removal ($P = 0.042$; odds ratio 12.095; 95% confidence interval 1.097-133.377) [Table 4].

Discussion

There are no objective criteria for when to remove silicone airway stents in benign airway stenosis. To the best of our knowledge, this is the first descriptive study of the timing of stent removal in PTBS. We analyzed 44 PTBS patients with incomplete bronchial stenosis, who underwent elective stent removal. All patients achieved substantial improvement in dyspnea and pulmonary function tests after stenting. Our data suggest that the restenosis rate is reduced significantly after stenting for at least 12 months in PTBS patients with incomplete stenosis.

Unlike PTBS patients with complete stenosis, patients with incomplete stenosis had a relatively favorable clinical course after stent removal.[9] We considered two probable

Table 3: Factors contributing to restenosis after stent removal

Variables	No restenosis (*n*=37)	Restenosis (*n*=7)	*P* value
Age, years	36 (32-46)	27 (24-39)	0.027
Female gender	29 (78)	7 (100)	0.318
Baseline pulmonary function tests			
FEV_1, % predicted	67 (63-71)	67 (58-76)	0.947
FVC, % predicted	81 (70-92)	85 (59-102)	0.841
FEV_1/FVC, %	66 (54-76)	63 (56-83)	0.911
Active TB	1 (3)	0 (0)	1.000
TB medication at first intervention	8 (22)	1 (14)	1.000
Duration of TB treatment, months	6 (6-11)	6 (6-12)	0.725
Interval from TB medication to intervention, months	48 (10-86)	7 (3-33)	0.057
Interval from symptom onset to intervention, months	4 (1-18)	5 (1-7)	0.975
Stenting site			
Left main bronchus	31 (84)	5 (71)	
Right main bronchus	3 (8)	0 (0)	0.241
Right bronchus intermedius	3 (8)	2 (29)	
Stent length, mm	45 (38-50)	40 (40-45)	0.469
Shortest diameter of stenosis, mm	1 (1-3)	1 (1-3)	0.925
Patients with additional interventions	22 (59)	4 (57)	1.000
Stent-related complication			
Mucostasis	5 (14)	2 (29)	0.318
Stent migration	15 (41)	3 (43)	1.000
Granulation tissue overgrowth	15 (41)	2 (29)	0.689
Duration of stenting >12 months	26 (70)	1 (14)	0.009

Values are expressed as numbers (percentage) or median (interquartile range). FEV_1 = Forced expiratory volume in 1 s, FVC = Forced vital capacity, TB = Tuberculosis

Table 4: Multiple logistic regression of restenosis after stent removal

Variables*	*P* value	Odds ratio	95% confidence interval
Age	0.125	0.900	0.787-1.030
Duration of stenting>12 months	0.042	12.095	1.097-133.377
Interval from TB medication to intervention	0.206	0.999	0.998-1.000

*Several variables were selected as covariates based on univariate analyses (age, interval from TB medication to intervention and 12 months of stenting).
TB =Tuberculosis

explanations: The integrity of cartilage structure is preserved in the incompletely stenosed bronchus and the individual healing response. *Mycobacterium tuberculosis* infection in the tracheobronchial tree leads to cartilage destruction, causing fibrotic stenosis.[13] More severe inflammation of the bronchial tree might be followed by a more severe stricture and greater cartilaginous damage. In PTBS patients, endobronchial inflammation severe enough to result in complete stenosis might cause severe bronchial cartilage damage; then, severe bronchomalacia might develop from the advanced cartilage loss after stent removal. Regarding the individual healing response, some patients might have increased healing responses. Once tissue damage occurs, the healing cascade starts, including regeneration, proliferation and remodeling; some reports suggested genetic susceptibility with aberrations in the healing process.[14,15] Applying these hypotheses to the bronchial damage resulting from *M. tuberculosis* infection, some patients with an aberrant or excessive healing process develop severe bronchial stenosis and restenosis develops after stent removal due to a persisting abnormal healing process. Therefore, when the pulmonary interventionist considers silicone stent removal, it might be reasonable to assess the severity of bronchial stenosis at the initial presentation.

Mechanical airway dilatation with ballooning, laser therapy or bougienation causes considerable mucosal trauma, followed by unpredictable healing and restenosis.[16-18] Therefore, the decision on stent removal should be based on whether the mucosal trauma to the stenotic segment, induced by mechanical dilatation, has fully recovered. In PTBS patients with incomplete bronchial obstruction, a great reduction was seen in the restenosis rate after stenting for 12 months; therefore, recovery of the mechanically dilated bronchus might take at least 12 months. As a result, we suggest that the elective removal of a bronchial silicone stent in PTBS patients with incomplete stenosis should be considered 12 months after stent placement.

There are clear limitations to this study. First, it had a retrospective design. The treatment plan was devised by a single interventional pulmonologist on a case-by-case basis. However, all procedures were performed by an interventional pulmonologist with 20 years of experience who consistently used standard methods. Further randomized prospective studies with different interventional bronchoscopists are required to establish objective criteria for elective stent removal in PTBS patients. Second, our results cannot be generalized to other airway stenoses besides PTBS. Finally, the current study was conducted with relatively small study population, which was due to the rarity of PTBS.

In conclusion, stent placement for longer than 12 months can reduce restenosis after stent removal in patients with incomplete PTBS.

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